

## IPK researchers reveal that timely KNL2 degradation is critical for maintaining genome stability

Gatersleben, 26.06.2025 **An international research team led by the IPK Leibniz Institute has uncovered the molecular mechanisms governing the post-translational regulation of the kinetochore protein KNL2 and its pivotal role in cell division. The findings, which were published in the journal “The Plant Cell”, provide essential insights into kinetochore biology in plants, with broader implications for understanding similar processes across other species.**

Accurate cell division is essential for the proper transmission of genetic information. Each chromosome contains a centromere, a region that is central in guiding chromosome movement during division. At the centromere, the kinetochore protein complex forms and acts as the attachment site for microtubules, the dynamic fibres that separate chromosomes into daughter cells. One key kinetochore protein, KNL2, supports the deposition of CENH3, a specialised histone that defines the centromere. Although the importance of KNL2 is well recognised, the mechanisms regulating its levels during the cell cycle have not been fully understood in plants and other organisms.

The team discovered that  $\alpha$ KNL2 of *Arabidopsis thaliana* is degraded during mitosis through ubiquitin-dependent proteolysis. In *A. thaliana* and the nematode *Caenorhabditis elegans*, protein interaction studies identified a link between KNL2 and the Anaphase-Promoting Complex, the Cyclosome (APC/C), a protein complex that triggers cell cycle progression by marking specific proteins for degradation. “Notably, we identified for the first time two key components of the APC/C, APC10 and CDC20.1, that directly interact with  $\alpha$ KNL2 to trigger its degradation”, says Manikandan Kalidass, first author of the study.

“The study also demonstrated that when the APC/C is disrupted or mutations prevent  $\alpha$ KNL2 from being degraded, the protein accumulates abnormally. This buildup causes errors in chromosome segregation and leads to major developmental problems”, says Dr. Inna Lermontova, head of IPK’s research group “Kinetochore-Biology”. Plants expressing a non-degradable form of  $\alpha$ KNL2 showed severe growth, fertility, and mitosis defects.

These findings illustrate a broader biological principle: proteins involved in the cell cycle must be tightly regulated, appearing and disappearing at the correct times. Degradation is vital in ensuring that proteins do not linger beyond their needed function. When this system fails, it can lead to serious consequences such as uncontrolled cell growth, a hallmark of cancer.

Looking ahead, the researchers plan to investigate how  $\alpha$ KNL2 degradation is fine-tuned under varying conditions, such as environmental stress or different developmental stages. In addition to ongoing collaborations focused on the *C. elegans* KNL2, the team also aims to expand its research network to include studies on KNL2 regulation in animals and humans, further broadening the impact of their findings across different biological systems.

### Press Release

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### Graphic: $\alpha$ KNL2 degradation during early mitosis

This model illustrates how the APC/C complex marks  $\alpha$ KNL2 excess for degradation in *A. thaliana*. By tagging specific sites on  $\alpha$ KNL2, the complex ensures timely removal, especially during early mitosis, to support proper cell division.

